Development of follow up recommendations for completely resected Gastroenteropancreatic Neuroendocrine Tumours (GER-NETS)

Practice Survey of Commonwealth Neuroendocrine Tumour Collaboration (CommNETS) in conjunction with North American Neuroendocrine Tumour Society (NANETS)

Simron Singh, MD, MPH
for the
CommNETS Follow up Working Group
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Presented at 2017 Gastrointestinal Cancers Symposium | #GI17
CommNETS

- Commonwealth Neuroendocrine Tumour Collaboration
- Established in 2015 between Australia, New Zealand and Canada
- Mission:
  - To improve the outcomes of NET patients through accelerated collaboration between patients, clinicians and researchers in member nations
- NET clinicians, researchers, patients/advocates
Background

- The incidence of neuroendocrine tumours (NETs) has doubled over the last 20 years.
- The optimal follow up protocol for fully resected GI-NETS is undetermined.
- CommNETS in collaboration with NANETS undertook the following study to develop consensus-based follow up guidelines for this population.
Why is optimal follow up important in NETs?

- Patient Centered Care
  - Stress, anxiety
  - Financial toxicity
  - Effect of excess imaging

Health System resources

Does follow up affect outcomes?
Methodological Approach

1. Systematic Literature Review
2. Current Practice Survey
3. Institute for Clinical Evaluative Sciences (ICES) Population Data Review
4. Appropriateness Delphi Survey
5. In-Person Recommendation Consensus Meeting
Medline search: 576 abstracts identified

Abstracts of meetings (ASCO, ESMO, NANETS, and ENETS)

Excluded:
Not relevant to follow up: 129
No original data collection: 38
< 25 patients: 22
Stage 4 disease: 176
Non NET cancer: 164
Duplicate: 11

39 articles for full text review

27 excluded as no follow up strategy described

12 articles

12 articles did not compare follow up

0 studies identified
Practice Survey: Aim

To characterize clinical practice follow up patterns for fully resected GEP NETs among Net treatment providers across Canada, US, Australia and New Zealand
Practice Survey Methods

- A detailed electronic cross-sectional survey was distributed to members of the CommNETS Collaboration (Australia, NZ, and Canada) and NANETS
  - Developed by expert panel based on clinical prognostic factors
  - Open response methodology
- Respondents were asked questions in 3 categories: background, general NET surveillance, and evaluation frequency of follow up
- Descriptive statistics were examined for all responses, stratified by country, patient volume and specialty
Practice Survey: Demographic Results

- N = 163
  - Australia: 59; NZ: 25; Canada: 46; US: 33
- 50% Medical Oncologists; 23% Surgeons; 13% Nuclear Medicine; 14% other
- 63.2% reported their institution did not follow any specific guidelines
Patient Volume

Respondents were asked about their current annual new patient volume and follow up patient volume.

<table>
<thead>
<tr>
<th>Patient Volume</th>
<th>Annual new patient volume</th>
<th>Follow up care for GEP-NETs per year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>0-4</td>
<td>26</td>
<td>16</td>
</tr>
<tr>
<td>5-10</td>
<td>43</td>
<td>26</td>
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<td>11-50</td>
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<td>34</td>
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<tr>
<td>51-100</td>
<td>17</td>
<td>10</td>
</tr>
<tr>
<td>&gt;100</td>
<td>21</td>
<td>13</td>
</tr>
</tbody>
</table>

For stratified analyses, follow up care patient volume was categorized as “low” (0-10), “medium” (11-50), and “high” (>51).
Reported Follow up frequency practice

Based on a fully resected G1 Tx N0 GI-NET

- 0-2y: 62% q24mo, 15% q12mo, 10% q6mo, 2% q3mo, 2% None
- 3-5y: 59% q24mo, 24% q12mo, 11% q6mo, 4% q3mo, 1% None
- >5y: 41% q24mo, 31% q12mo, 10% q6mo, 9% q3mo, 1% None, 0% Other

CommNETS
Commonwealth Neuroendocrine Tumour Collaboration
Top 5 Ranked Prognostic Factors

1. Grade
2. Ki67/mitotic count
3. T stage/size
4. N stage/nodal status
5. Site of origin
# Years of follow up prior to discharge

<table>
<thead>
<tr>
<th>Follow up time (years)</th>
<th>Total</th>
<th>Patient Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Low (0-10)</td>
</tr>
<tr>
<td>&lt;4</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>5%</td>
<td>6%</td>
</tr>
<tr>
<td>5</td>
<td>39</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>28%</td>
<td>33%</td>
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<tr>
<td>6 to 10</td>
<td>36</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>26%</td>
<td>22%</td>
</tr>
<tr>
<td>&gt;10</td>
<td>32</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>23%</td>
<td>22%</td>
</tr>
<tr>
<td>Other</td>
<td>25</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>18%</td>
<td>18%</td>
</tr>
</tbody>
</table>

*excludes follow up related to an underlying endocrine or other syndrome for ‘non-relapse’*
Influence of grade

Would G2 Histology affect your follow up?

- No changes
- More tx
- More visits
- More tx and visits
- Less tx
- Less visits
- Less tx and visits
- Other

Would G3 Histology affect your follow up?

- No changes
- More tx
- More visits
- More tx and visits
- Less tx
- Less visits
- Less tx and visits
- Other
Influence of nodal status and primary site?

**Positive lymph nodes (N1)**

- No changes
- More lx
- More visits
- More lx and visits
- Less lx
- Less visits
- Less lx and visits
- Other

**Pancreatic primary**

- No changes
- More lx
- More visits
- More lx and visits
- Less lx
- Less visits
- Less lx and visits
- Other
Summary of survey findings

- No evidence for optimal frequency and modality of NET follow up has been established in the literature
- No consensus exists in current practice for follow up of resected NETs in regards to
  - Frequency
  - Modality of follow up
- There is a need to define a standard, evidence-based program for follow up to optimize patient experience and resource utilization
How does follow up modality change over time?

- Endoscopy
- US
- CT
- MRI
- Functional imaging
- CgA
- Urinary 5-HIAA
- NSE
- Respective hormones for functional NETs
- None
- Other

Legend:
- >5y
- 3-5y
- 2y
ICES
Institute for Clinical & Evaluative Sciences (ICES) Database Results
Administrative Database Review

- Setting: Ontario, Canada (pop. ~15.5M, ~80K new cancer cases/year)
- Population: Adults >18 years, with a curative, resected GI NET diagnosed between January 1, 1994 – December 31, 2012
- Index date = GI NET diagnosis date
- Total N = 1048
Recurrence-free survival probability censoring death
N=1,048

Med = 9.47 years

Years of follow up
Recurrence-free survival probability censoring death

N=1,048

Med = 9.47 years

Years of follow up
Combined number of abdomen CT, MRI and Ultrasound per 100 patient-days in each time period

Number of scans per 100 patient-days

- Months 1-3
- Months 4-6
- Months 7-9
- Months 10-12
- Months 13-15
- Months 16-18
- Months 19-21
- Months 22-24
- Months 25-36
- Months 37-48
- Months 49-60
- Months 61-72
- Months 73-84
- Months 85-96
- Months 97-108
- Months 109-120
- Months 121-252
Methods

- Utilizing a RAND/UCLA appropriateness methodology (RAM)
- Multidisciplinary expert panel of 18 physicians and patient rep scored 193 follow up care scenarios for GI-NETS using an online survey.
- Appropriateness for frequency and investigations for follow up were scored from 1 to 9.
- Median appropriateness scores from 1-3 were considered inappropriate, 4-6 uncertain, and 7-9 appropriate. (defined as: “the expected health benefit of an intervention exceeding the expected negative consequences by a wide enough margin that the procedure is worth doing, regardless of cost” Brook, RH., 1986)
- Consensus was reached when 75% of expert panelists were in agreement.
Acknowledgements

• CommNETS members, executive and staff
• NANETS members, executive and staff
• ICES research team